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LETTER

Thought on "Isolation and Phenotypic Characterization of Virulent Bacteriophages Against Multidrug-Resistant Escherichia Coli and Its Phage-Resistant Variant from Sewage Sources" [Letter]

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Dear editor

We have read the article written by Fikadu et al, in which they isolated and phenotypically characterized phages that infect multidrug-resistant (MDR) *Escherichia coli*.[1] The emergence of MDR-*E. coli* has garnered significant attention in several countries, necessitating alternative therapies to address this issue.[2,3] One such approach is the utilization of phage therapy. However, as highlighted by the authors in their article, the emergence of phage-resistant variants presents a new challenge, thus underscoring the perceived necessity of employing phage cocktails as a therapy strategy. This article provides a good initial step toward conducting further studies related to the utilization of phage cocktails for the treatment of bacterial infections. However, upon a more thorough review of this article, several suggestions for improving future studies are provided.

This study did not clearly disclose the method used to identify MDR in *E. coli*. The employment of minimum inhibitory concentration (MIC) method is favored as it is deemed more effective, as it can also identify the lowest concentration of antibiotics required to kill the pathogen. Moreover, the negative control used in this study should be consistent with the suspension in which the phage was suspended. The negative control should also have been loaded on the same plate in Figure 4 for a better comparison. Since the study focuses on phenotypic characterization, it would be beneficial for the authors to include electron microscopy (EM) data of the phages to determine if there are any morphological differences among the three phages. This could serve as a basis for understanding the antagonistic effect of the phage cocktail on phage-resistant variants, as discussed in the previous study, which indicated that antagonistic interactions are influenced by several factors, including phage types.[4] Phenotypic analysis can also be conducted on phage-resistant strains to observe whether there are any phenotypic changes in the colonies formed on agar plates compared to the wild-type. For example, the mucoid shiny appearance, attributed to the overproduction of exopolysaccharide (EPS), acts as a physical barrier against phage infection, while edgy morphotype indicates increased expression of curli fimbriae and cellulose matrix components.[5] This is a crucial step towards understanding phage resistance mechanisms for future research endeavors. Phage cocktail therapy is considered a promising approach to improving and overcoming the occurrences of phage-resistant variants. However, this recent study reveals that this may not always work, as evidenced by the antagonistic effects of the phage cocktail on the phage-resistant variants. It would also be more convincing to conduct sequential exposure during infection rather than combining all three phages simultaneously from the initial infection for comparison. In addition, it is important to note that the absence of plaque formation does not necessarily indicate resistance to the phage. Therefore, the authors could conduct an experiment involving the

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examination of the lysis curve of each host when challenged either with single or phage cocktails within the specified timeframe while also considering the multiplicity of infection (MOI) applied. This would allow us to understand how the phage–bacterium ratio influences the dynamics of bacterial lysis and develops more effective treatment strategies against bacterial infections.

Disclosure

The authors report no conflicts of interest in this communication.

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